COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.15	0.15

FILE 'MEDLINE' ENTERED AT 12:02:18 ON 26 JUL 2000

FILE 'CAPLUS' ENTERED AT 12:02:18 ON 26 JUL 2000
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

=> s vacomycine and toleran?

L1 0 VACOMYCINE AND TOLERAN?

=> s vacomycine and

MISSING TERM AFTER ACOMYCINE AND
Operators must be followed by a search term, L-number, or query name.

=>

=> s vancomycine and toleran?

L2 3 VANCOMYCINE AND TOLERAN?

=> s vancomycin and toleran?

L3 168 VANCOMYCIN AND TOLERAN?

=> s pneumoniae and l3

L4 14 PNEUMONIAE AND L3

=> rem dup l4

DUP IS NOT VALID HERE
The DELETE command is used to remove various items stored by the system.

To delete a saved query, saved answer set, saved L-number list, SDI request, batch request, mailing list, or user-defined cluster, format, or search field, enter the name. The name may include ? for left, right, or simultaneous left and right truncation.

Examples:

```
DELETE BIO?/Q           - delete query names starting with BIO
DELETE ?DRUG/A          - delete answer set names ending with DRUG
DELETE ?ELEC?/L         - delete L-number lists containing ELEC
DELETE ANTICOAG/S       - delete SDI request
DELETE ENZYME/B         - delete batch request
DELETE .MYCLUSTER       - delete user-defined cluster
DELETE .MYFORMAT        - delete user-defined display format
DELETE .MYFIELD         - delete user-defined search field
DELETE NAMELIST MYLIST - delete mailing list
```

To delete an ordered document or an offline print, enter its number.

Examples:

```
DELETE P123001C         - delete print request
DELETE D134002C         - delete document order request
```

To delete an individual L-number or range of L-numbers, enter the L-number or L-number range. You may also enter DELETE LAST followed by a number, n, to delete the last n L-numbers. RENUMBER or NORENUMBER may also be explicitly specified to override the value of SET RENUMBER.

Examples:

```
DELETE L21              - delete a single L-number
DELETE L3-L6            - delete a range of L-numbers
DELETE LAST 4           - delete the last 4 L-numbers
DELETE L33-             - delete L33 and any higher L-number
DELETE -L55             - delete L55 and any lower L-number
DELETE L2-L6 RENUMBER - delete a range of L-numbers and
                          renumber remaining L-numbers
DELETE RENUMBER         - renumber L-numbers after deletion of
                          intermediate L-numbers
```

Entire sets of saved items, SDI requests, batch requests, user-defined items, or E-numbers can be deleted.

Examples:

```
DELETE SAVED/Q - delete all saved queries
DELETE SAVED/A - delete all saved answer sets
DELETE SAVED/L - delete all saved L-number lists
DELETE SAVED   - delete all saved queries, answer sets,
                 and L-number lists
DELETE SAVED/S - delete all SDI requests
DELETE SAVED/B - delete all batch requests
DELETE CLUSTER - delete all user-defined clusters
DELETE FORMAT  - delete all user-defined display formats
DELETE FIELD   - delete all user-defined search fields
DELETE SELECT  - delete all E-numbers
DELETE HISTORY - delete all L-numbers and restart the
                 session at L1
```

To delete an entire multifile SDI request, enter DELETE and the name of the request. To delete a component from the multifile SDI, enter DELETE and the name of the component.

```
=> dup rem l4

PROCESSING COMPLETED FOR L4
L5            11 DUP REM L4 (3 DUPLICATES REMOVED)

=> d l5 1-11 bib ab


L5   ANSWER 1 OF 11  MEDLINE
AN   2000254397     MEDLINE
DN   20254397
TI   [Mycoplasma pneumoniae pneumonia in a four-year-old child with
     transient abscess in the right lower lobe].
     Pneumopathie `a Mycoplasma pneumoniae chez un enfant de quatre
     ans avec abcedation bulleuse transitoire du lobe inferieur droit.
AU   Siret D; Picherot G
CS   Service de pediatrie generale, Hopital M`ere et Enfant, Nantes, France.
SO   ARCHIVES DE PEDIATRIE, (2000 Apr) 7 (4) 391-5.
     Journal code: BWH. ISSN: 0929-693X.
CY   France
DT   Journal; Article; (JOURNAL ARTICLE)
LA   French
FS   Priority Journals
EM   200009
```

EW 20000901
AB The frequency of [redacted]coplasma **pneumoniae** infection a[redacted]g community-acquired pneumonia, underestimated for a long time, is now better known. Severe evolution is yet uncommon. Differential diagnosis with Streptococcus **pneumoniae** is often difficult. CASE REPORT: A 4-year-old child was admitted for a right lower lobe pneumonia, with very high values of white blood cell count and CRP, worsening despite a treatment with high doses of amoxicillin, then with cefotaxime and **vancomycin**. Diagnosis of M. **pneumoniae** infection was considered only on the tenth day after admission and confirmed on the thirteenth day. Clinical outcome rapidly improved with macrolide antibiotherapy. Radiologic outcome consisted, two months after the beginning of the pneumonia, in abscess of the right lower lobe, which recovered in one month with continuing oral antibiotherapy. CONCLUSION: Lung abscess is very rare in M. **pneumoniae** pneumonia, as only two other cases were described in the literature. In all three cases, macrolide therapy was delayed. Those cases highlight the importance of considering M. **pneumoniae** infection in a beta-lactams-resistant community-acquired pneumonia, whatever its severity may be, and to start macrolide antibiotherapy. Our case also shows the possibility of a conservative treatment in case of pulmonary abscess, if clinical **tolerance** is good.

L5 ANSWER 2 OF 11 MEDLINE
AN 2000087038 MEDLINE
DN 20087038
TI Isolation and characterization of **vancomycin-tolerant** Streptococcus **pneumoniae** from the cerebrospinal fluid of a patient who developed recrudescent meningitis.
AU McCullers J A; English B K; Novak R
CS Department of Infectious Diseases, St. Jude Children's Research Hospital; Division of Infectious Diseases, Center, Memphis, Tennessee, USA.. jon.mccullers@stjude.org
NC AI-08831 (NIAID)
CA-21765 (NCI)
SO JOURNAL OF INFECTIOUS DISEASES, (2000 Jan) 181 (1) 369-73.
Journal code: IH3. ISSN: 0022-1899.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200005
EW 20000502
AB The emergence of **tolerance** to **vancomycin** has recently been reported in Streptococcus **pneumoniae**, the most common cause of bacterial meningitis. A **vancomycin**- and cephalosporin-**tolerant** strain of S. **pneumoniae**, the Tupelo strain, was isolated from the cerebrospinal fluid of a patient who then developed recrudescence of meningitis despite treatment with **vancomycin** and a third-generation cephalosporin. The Tupelo strain evidenced no lysis in the exponential or stationary phase of growth when exposed to **vancomycin** and only minimal loss of viability. Further characterization revealed normal autolysin expression, localization, and triggering by detergents, indicating that the defect leading to **tolerance** in the Tupelo strain is in the control pathway for triggering of autolysis. Because **tolerance** is a precursor phenotype to resistance and may lead to clinical failure of antibiotic therapy, these observations may have important implications for **vancomycin** use in infections caused by S. **pneumoniae**.

L5 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2000 ACS
AN 1999:723180 CAPLUS
DN 131:347526
TI Pneumococcus-inhibiting peptide antibiotics, ABC transporter and

two-component signal transduction system and genes of Streptococcus and uses thereof

IN Novak, Rodger; Tuomanen, Elaine I.

PA St. Jude Children's Research Hospital, USA

SO PCT Int. Appl., 151 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9957281	A2	19991111	WO 1999-US9792	19990506
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9937860	A1	19991123	AU 1999-37860	19990506

PRAI US 1998-73541 19980506
WO 1999-US9792 19990506

AB The present invention discloses antibiotic peptides, including naturally occurring peptides. The present invention also includes the nucleic acid sequences encoding such peptides and the corresponding amino acid sequences. Methods of identifying, making, and using the antibiotic peptides are also disclosed. The present invention further provides genes (vex1, vex2, vex3, vncS, vncR) and proteins (ABC transporter, histidine kinase, response regulator) involved in the regulation of bacterial autolysis. Thus, a 25-30-amino acid peptide which kills autolysis-prone pneumococci without lysis was identified. The gene for this peptide, p28, was cotranscribed with 3 genes encoding an ABC transporter, and was followed by 2 genes encoding a two-component signal transduction system. Bacteria with mutant, inactivated vex genes were not inhibited by the antibiotic peptide. Similarly, inactivated vncR and/or vncS genes prevented the antibiotic activity of the peptide. Penicillin- and **vancomycin-tolerant** Streptococcus mutants in vex1, vncS or vncR were prepd. These strains may be useful in screening for novel antibiotics effective against penicillin and/or **vancomycin-tolerant** bacterial strains.. SSCP anal. indicated that an antibiotic-**tolerant** Streptococcus harbored a vncS with two basepair differences from the antibiotic-sensitive strain.

L5 ANSWER 4 OF 11 MEDLINE DUPLICATE 1

AN 1999303093 MEDLINE

DN 99303093

TI Emergence of **vancomycin tolerance** in Streptococcus **pneumoniae** [see comments].

CM Comment in: Nature 1999 Jun 10;399(6736):590-3
Comment in: Nature 1999 Jun 10;399(6736):524-5, 527

AU Novak R; Henriques B; Charpentier E; Normark S; Tuomanen E

CS Dept of Infectious Diseases, St. Jude Children's Research Hospital, Memphis, Tennessee 38105, USA.

SO NATURE, (1999 Jun 10) 399 (6736) 590-3.
Journal code: NSC. ISSN: 0028-0836.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals; Cancer Journals

OS GENBANK-AF140356

EM 199909

EW 19990901
AB Streptococcus **pneumoniae**, the pneumococcus, is the most common cause of sepsis and meningitis. Multiple-antibiotic-resistant strains are widespread, and **vancomycin** is the antibiotic of last resort. Emergence of **vancomycin** resistance in this community-acquired bacterium would be catastrophic. Antibiotic **tolerance**, the ability of bacteria to survive but not grow in the presence of antibiotics, is a precursor phenotype to resistance. Here we show that loss of function of the VncS histidine kinase of a two-component sensor-regulator system in S. **pneumoniae** produced **tolerance** to **vancomycin** and other classes of antibiotic. Bacterial two-component systems monitor environmental parameters through a sensor histidine-kinase/phosphatase, which phosphorylates/dephosphorylates a response regulator that in turn mediates changes in gene expression. These results indicate that signal transduction is critical for the bactericidal activity of antibiotics. Experimental meningitis caused by the vncS mutant failed to respond to **vancomycin**. Clinical isolates **tolerant** to **vancomycin** were identified and DNA sequencing revealed nucleotide alterations in vncS. We conclude that broad antibiotic **tolerance** of S. **pneumoniae** has emerged in the community by a molecular mechanism that eliminates sensitivity to the current cornerstone of therapy, **vancomycin**.

L5 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2000 ACS
AN 1998:621235 CAPLUS
DN 129:254975
TI Compositions and methods for treating infections using cationic peptides alone or in combination with antibiotics
IN Fraser, Janet R.; West, Michael H. P.; Mcnicol, Patricia J.
PA Micrologix Biotech Inc., Can.
SO PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9840401	A2	19980917	WO 1998-CA190	19980310
	WO 9840401	A3	19981217		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9866047	A1	19980929	AU 1998-66047	19980310
	EP 966481	A2	19991229	EP 1998-907779	19980310
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI US 1997-40649 19970310
US 1997-915314 19970820
US 1997-60099 19970926
US 1998-30619 19980225
WO 1998-CA190 19980310

AB Compns. and methods for treating infections, esp. bacterial infections, are provided. Cationic peptides in combination with an antibiotic agent are administered to a patient to enhance the activity of the antibiotic agent, overcome **tolerance**, and overcome acquired or inherent resistance. Thus, a combination of antimicrobial agent and cationic peptide that breaks **tolerance** results in a decrease of min. bacterial concn. (MBC) to min. inhibitory concn. (MIC) ratio to <32. The

combination of va[redacted]omycin and MBI 26 overcomes the [redacted] tolerance of Ente[redacted]coccus casseliflavus and E. fae[redacted]is with MBC/MIC ratio of 1-8 compared to that of 32 to >256 for **vancomycin** alone.

L5 ANSWER 6 OF 11 MEDLINE
AN 97425455 MEDLINE
DN 97425455
TI Trovafloxacin.
AU Haria M; Lamb H M
CS Adis International Limited, Auckland, New Zealand.
SO DRUGS, (1997 Sep) 54 (3) 435-45; discussion 446. Ref: 48
Journal code: EC2. ISSN: 0012-6667.
CY New Zealand
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199712
EW 19971204
AB Trovafloxacin is a fluoroquinolone antibacterial agent with a broad spectrum of activity. Trovafloxacin has similar or 2-fold lower activity than ciprofloxacin against Enterobacteriaceae and Pseudomonas aeruginosa. Against Haemophilus influenzae and Moraxella catarrhalis, trovafloxacin has similar activity to ciprofloxacin. Other susceptible Gram-negative pathogens include Neisseria gonorrhoeae, Chlamydia trachomatis and mycoplasmas. The drug is active against Gram-positive bacteria and consistently displayed greater activity (2- to 8-fold) than ciprofloxacin against all staphylococci and streptococci tested; activity included methicillin-resistant staphylococci and penicillin-resistant Streptococcus **pneumoniae**. Trovafloxacin has some activity against **vancomycin**-resistant enterococci. Anaerobes such as Bacteroides and Clostridium spp. are also susceptible to trovafloxacin. Preliminary clinical data suggest that trovafloxacin is effective in the treatment of patients with upper and lower respiratory tract and uncomplicated urinary tract infections and infections caused by C. trachomatis or N. gonorrhoeae. The most frequently noted adverse event with trovafloxacin is dizziness which is reported in 11% of patients versus 3% of those receiving comparator agents. Other commonly reported events (> 1% of patients) are nausea, headache, vomiting, vaginitis and diarrhoea.

L5 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2000 ACS
AN 1997:274500 CAPLUS
DN 126:321006
TI Formulation of a flush solution of heparin, **vancomycin**, and colistin for implantable access systems in oncology
AU Vincentelli, J.; Braguer, D.; Guillet, P.; Delorme, J.; Carles, G.; Perez, R.; Duffaud, F.; Nicoara, A.; Drancourt, M.; Favre, R.; Crevat, A.
CS Pharmacy CHU Timone, Marseille, 13385, Fr.
SO J. Oncol. Pharm. Pract. (1997), 3(1), 18-23
CODEN: JOPPFI; ISSN: 1078-1552
PB Appleton & Lange
DT Journal
LA English
AB Because of the increased use of implantable access systems, the incidence of bloodstream and catheter infections assocd. with these systems has concomitantly increased. Classically, heparin-lock flush solns. were used to prevent thrombosis; more recently, **vancomycin** was added to the soln. to prevent infections caused by Gram-pos. bacteria, particularly

coagulase-neg. Staphylococci. Disorders due to Gram-neg. organisms have now appeared in [redacted]l. patients. The authors [redacted]re tested the addn. of colistin to heparin-**vancomycin** solns. Colistin was chosen for its good activity against Gram-neg. bacteria (98% susceptibility in our hospital), its good **tolerance** due to low systemic passage, and its low cost. The authors developed formulations contg. heparin (100 IU/mL) and various concns. of **vancomycin** (10-500 .mu.g/mL) and colistin (10-100 .mu.g/mL) in 0.9% NaCl. Each sterile soln. was tested for phys. and chem. compatibility (spectrophotometry, NMR, and pH measurements) and its antibacterial activity (against oxacillin-resistant Staphylococcus aureus, Enterococcus faecium, Klebsiella **pneumoniae** -exhibiting broad-spectrum .beta.-lactamase (BSBL), imipenem-resistant Pseudomonas aeruginosa) for 2 mo at 4.degree. and at room temp. The most suitable combination of drugs is heparin (100 IU/mL), **vancomycin** (100 .mu.g/mL), and colistin (100 .mu.g/mL). This flush soln. maintains activity when stored at 4.degree.C for up to 1 mo. The combination of heparin, **vancomycin**, and colistin can be used as a flush soln. for indwelling catheters.

L5 ANSWER 8 OF 11 MEDLINE
AN 96427729 MEDLINE
DN 96427729
TI The comparative antimicrobial activity of levofloxacin tested against 350 clinical isolates of streptococci.
AU Biedenbach D J; Jones R N
CS Department of Pathology, University of Iowa College of Medicine, Iowa City 52242, USA.
SO DIAGNOSTIC MICROBIOLOGY AND INFECTIOUS DISEASE, (1996 May) 25 (1) 47-51.

Journal code: DMI. ISSN: 0732-8893.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199702
EW 19970204
AB The global trend of increasing **tolerance** and outright resistance to penicillin among streptococcal species becomes even more problematic when considering the coresistance patterns to other commonly used alternative therapies. Levofloxacin is a fluoroquinolone with excellent bioavailability properties that affords potential use in the treatment of a wide variety of infections caused by Gram-positive organisms such as streptococci. We evaluated the antistreptococcal activity (350 strains) of levofloxacin compared with other fluoroquinolones, beta-lactams (penicillin and cephalosporins), erythromycin, and **vancomycin** against beta- and alpha-hemolytic streptococci including penicillin-resistant strains of pneumococci and species within the viridans group. With the exception of one strain, all isolates were inhibited by levofloxacin concentrations of < or = 2 micrograms/ml including all penicillin-resistant viridans group and pneumococcal strains. This activity was superior to that of comparison fluoroquinolones, all beta-lactams, and erythromycin, whereas all strains remained susceptible to **vancomycin**. Time-kill results established that levofloxacin is bactericidal against most streptococci and has enhanced activity when combined with gentamicin. These results suggest that levofloxacin alone or in combination with an aminoglycoside may prove useful as an alternative to conventional therapeutic approaches of commonly encountered or serious streptococcal infections.

L5 ANSWER 9 OF 11 MEDLINE DUPLICATE 2
AN 96045145 MEDLINE
DN 96045145
TI Clinical experience with ceftriaxone treatment in the neonate.

AU Van Reempts P J; [redacted] Overmeire B; Mahieu L M; Vana[redacted]er K J
CS Department of Pe[redacted]trics, University Hospital of A[redacted]erp, Belgium..
SO CHEMOTHERAPY, (1995 Jul-Aug) 41 (4) 316-22.
Journal code: D15. ISSN: 0009-3157.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199601
AB The safety of ceftriaxone has been evaluated in 80 neonates who were treated empirically for suspected infection with either ceftriaxone and ampicillin (group A, age 0-72 h) or ceftriaxone and **vancomycin** (group B, age greater than 72 h). Within 48 h after birth 2 group A patients died from sepsis (Haemophilus influenzae, Streptococcus **pneumoniae**, 1 case each); 1 group B patient died from sepsis (Pseudomonas aeruginosa). All bacterial isolates from group A patients were susceptible to ceftriaxone, but in 4 of the 8 group B patients with positive cultures a change in antibiotic therapy was required. Eosinophilia, thrombocytosis and an increase in serum alkaline phosphatases were observed in a limited number of patients during and after discontinuation of treatment. Direct hyperbilirubinemia (> 2 mg/dl) occurred in 2 cases during treatment. Gallbladder sludge was sonographically diagnosed in 6 patients, but disappeared within 2 weeks after detection. One neonate had exanthema. Nurses rated ease of administration as very good. Ceftriaxone appears to be an interesting alternative in the empiric antibiotic treatment in the early neonatal period.

L5 ANSWER 10 OF 11 MEDLINE
AN 87288646 MEDLINE
DN 87288646
TI [Treatment of febrile episodes in neutropenic children by ceftazidime combined with netilmicin. Results of a multicenter study apropos of 88 cases].
Traitement des episodes febriles chez les enfants neutropeniques par la ceftazidime associee `a la netilmicine. Resultats d'une etude multicentrique `a propos de 88 observations.
AU Leverger G; Demeocq F; Harousseau J L; Taboureau O; Vannier J P; Boilletot A; de Lumley L; Boutard P; Olive D; Reinert P; et al
SO PATHOLOGIE BIOLOGIE, (1987 May) 35 (5) 648-51.
Journal code: OSG. ISSN: 0369-8114.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
LA French
FS Priority Journals
EM 198711
AB Infection is the most important cause of mortality in leucopenic patients.
A broad spectrum antibiotic therapy is imperative in febrile and neutropenic patients. In a multicentric study we have used ceftazidime (100 mg/kg/d) and netilmicin (6 mg/kg/d) in 88 children (fever greater than or equal to 38.5 degrees C, neutropenia less than 500/mm3) treated for acute leukemias (59), non Hodgkin lymphomas (13) or solid tumors (16).
Median age was 7 years (2 months-16 years). In patients who continued to remain febrile, **vancomycin** (40 mg/kg/d) was added after 48 hours. The effective treatment was continued until a neutrophil count greater than 1,000/mm3. The first combination (ceftazidime + netilmicin) was effective in 64 children (73%) and the second combination (ceftazidime + netilmicin + **vancomycin**) in 11 patients. Bacteria were isolated in 39 children: Escherichia coli: 9, Staphylococcus epidermidis: 9, Staphylococcus aureus: 8, Streptococcus: 6, Pseudomonas aeruginosa: 3,

Streptococcus **pneumoniae**: 1, Haemophilus: 1, Klebsiella **pneumoniae**: 1, Proteus: 1, Serratia: 1, Flavobacterium: 1. In these 39 patients, 30 became apyretic with ceftazidime and netilmicin and 6 after **vancomycin**. All blood culture were negative after the first combination. The median duration of antibiotic therapy was 14 days (5-9 days: 28, 10-20 days: 43, greater than 20 days: 17). There were no death, no superinfection. **Tolerance** was good without kidney or liver or biological perturbation. We conclude that the combination ceftazidime and netilmicin is effective in neutropenic children.

L5 ANSWER 11 OF 11 MEDLINE DUPLICATE 3
AN 81026178 MEDLINE
DN 81026178
TI Antibiotic-**tolerant** mutants of Streptococcus **pneumoniae** that are not deficient in autolytic activity.
AU Williamson R; Tomasz A
NC AI 16170 (NIAID)
SO JOURNAL OF BACTERIOLOGY, (1980 Oct) 144 (1) 105-13.
Journal code: HH3. ISSN: 0021-9193.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198102
AB Several mutants of Streptococcus **pneumoniae** were isolated that appeared **tolerant**, to varying extents, to the lytic and bactericidal effects of some antibiotics that inhibit peptidoglycan synthesis, but were not deficient in autolytic activity. The method used to select the mutants was based on the survival of **tolerant** mutants during treatment with either bacitracin, benzylpenicillin, D-cycloserine plus beta-chloro-D-alanine, or **vancomycin**. Most (60 to 80%) of the surviving isolates were found to be deficient in autolytic activity, and these were rejected. The smaller proportion that had wild-type sensitivity to deoxycholate-induced lysis was studied further with respect to **tolerance** to the other antibiotics used in the selection procedures. Two of these mutants (selected by treatment with benzylpenicillin) were **tolerant** to either benzylpenicillin or D-cycloserine plus beta-chloro-D-alanine, but were supersusceptible, in terms of initiation of lysis, to either bacitracin or **vancomycin**. The minimal inhibitory concentration values of several antibiotics for these two mutants were identical to those for the wild-type strain. Moreover, the interaction of radioactive benzylpenicillin with the penicillin-binding proteins, examined in whole organisms, also appeared the same as previously found for either wild-type or autolytic-deficient strains of S. **pneumoniae**.

waiting for full artical

AN 1999279565 MEDLINE
DN 99279565
TI A fission yeast gene (prr1(+)) that encodes a response regulator implicated in oxidative stress response.
AU Ohmiya R; Kato C; Yamada H; Aiba H; Mizuno T
CS Laboratory of Molecular Microbiology, School of Agriculture, Nagoya University, Chikusa-ku, Nagoya, 464-8601, Japan.
SO JOURNAL OF BIOCHEMISTRY, (1999 Jun) 125 (6) 1061-6.
Journal code: HIF. ISSN: 0021-924X.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AL031543; GENBANK-Z98978; GENBANK-AL034352
EM 200001
EW 20000104
AB An inspection of the Schizosaccharomyces pombe genome database revealed that this eukaryotic microorganism possesses a gene that may encode a bacterial type of histidine-to-aspartate (**His-Asp**) **phosphorelay** component, namely, a response regulator. The predicted gene, named prr1(+) (S. pombe response regulator), encodes a protein that contains a typical phospho-accepting receiver domain, preceded by a mammalian heat shock factor (HSF)-like DNA-binding domain. Inactivation of this prr1(+) gene resulted in mutant cells **defective** in some aspects of stress responses, including sensitivity to oxidative stress, cold-temperature, and heavy metal toxicity. It was also demonstrated that Prr1 is required for the transcription of some genes (e.g., trr1(+), ctt1(+)), which are induced by oxidative stress. These results suggest that a **His-Asp** **phosphorelay** system may be involved in a stress-activated signaling pathway in S. pombe.

L16 ANSWER 2 OF 4 MEDLINE DUPLICATE 2
AN 1998283999 MEDLINE
DN 98283999
TI Two-domain reconstitution of a functional protein histidine kinase.
AU Park H; Saha S K; Inouye M
CS Department of Biochemistry, University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School, 675 Hoes Lane, Piscataway, NJ 08854-5635, USA.
NC GM 19043 (NIGMS)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1998 Jun 9) 95 (12) 6728-32.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199809
EW 19980902
AB In prokaryotes, in the **absence** of protein serine/threonine/tyrosine kinases, protein histidine kinases play a major role in signal transduction involved in cellular adaptation to various environmental changes and stresses. Histidine kinases phosphorylate their cognate response regulators at a specific aspartic acid residue with ATP in response to particular environmental signals. In this **His-Asp phosphorelay** signal transduction system, it is still unknown how the histidine kinase exerts its enzymatic function. Here we demonstrate that the cytoplasmic kinase domain of EnvZ, a transmembrane osmosensor of Escherichia coli can be further divided into two distinct functional subdomains: subdomain A [EnvZ(C). (223-289); 67 residues] and subdomain B [EnvZ(C).(290-450); 161 residues]. Subdomain A, with a high helical content, contains the autophosphorylation site, H-243, and forms a

stable dimer havi[redacted] the recognition site for OmpR, [redacted]he cognate response regulator of Env[redacted]ubdomain B, an alpha/beta-prot[redacted], exists as a monomer. When mixed, the two subdomains reconstitute the kinase function to phosphorylate subdomain A at His-243 in the presence of ATP. Subsequently, the phosphorylated subdomain A is able to transfer its phosphate group to OmpR. The two-domain structure of this histidine kinase
provides an insight into the structural arrangement of the enzyme and its transphosphorylation mechanism.

L16 ANSWER 3 OF 4 MEDLINE DUPLICATE 3
AN 1998149313 MEDLINE
DN 98149313
TI An Escherichia coli protein that exhibits phosphohistidine phosphatase activity towards the HPt domain of the ArcB sensor involved in the multistep **His-Asp phosphorelay**.
AU Ogino T; Matsubara M; Kato N; Nakamura Y; Mizuno T
CS Laboratory of Molecular Microbiology, School of Agriculture, Nagoya University, Japan.
SO MOLECULAR MICROBIOLOGY, (1998 Feb) 27 (3) 573-85.
Journal code: MOM. ISSN: 0950-382X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-D86298
EM 199806
EW 19980604
AB The Escherichia coli sensory kinase, ArcB, possesses a histidine-containing phosphotransfer (HPt) domain, which is implicated in the **His-Asp** multistep **phosphorelay**. We searched for a presumed phosphohistidine phosphatase, if present, which affects the function of the HPt domain through its dephosphorylation activity. Using in vivo screening, we first identified a gene that appeared to interfere with the **His-Asp phosphorelay** between the HPt domain and the receiver domain of OmpR, provided that the gene product was expressed through a multicopy plasmid. The cloned gene (named sixA) was found to encode a protein consisting of 161 amino acids, which has a noticeable sequence motif, an arginine-histidine-glycine (RHG) signature, at its N-terminus. Such an RHG
signature, which presumably functions as a nucleophilic phosphoacceptor, was previously found in a set of divergent enzymes, including eukaryotic fructose-2,6-bisphosphatase, E. coli periplasmic phosphatase and E. coli glucose-1-phosphate phosphatase, and ubiquitous phosphoglycerate mutase. Otherwise, the entire amino acid sequences of none of these enzymes resembles that of SixA. It was demonstrated in vitro that the purified SixA protein exhibited the ability to release the phosphoryl group from the HPt domain of ArcB, but the mutant protein **lacking** the crucial histidine residue in the RHG signature did not. Evidence was also provided that a deletion mutation of sixA on the chromosome affected the in vivo phosphotransfer signalling. These results support the view that SixA is capable of functioning as a phosphohistidine phosphatase that may be implicated in the **His-Asp phosphorelay** through regulating the phosphorylation state of the HPt domain.

L16 ANSWER 4 OF 4 MEDLINE DUPLICATE 4
AN 97115827 MEDLINE
DN 97115827
TI Nucleoside-diphosphate kinase-mediated signal transduction via histidyl-aspartyl **phosphorelay** systems in Escherichia coli.
AU Lu Q; Park H; Egger L A; Inouye M
CS Department of Biochemistry, Robert Wood Johnson Medical School, Piscataway, New Jersey 08854, USA.
NC GM19043 (NIGMS)

SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Dec 20) 271 (51) 32886-93.
Journal code: HIV ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199703
EW 19970304
AB Nucleoside-diphosphate kinase (NDP kinase), a key enzyme in nucleotide metabolism, is also known to be involved in growth and developmental control and tumor metastasis suppression. Interestingly, we find that coexpression of NDP kinase with Taz1, a Tar/EnvZ chimera, in the **absence** of its native signal, can activate a porin gene ompC-lacZ expression in Escherichia coli. Further studies show that NDP kinase can act as a protein kinase to phosphorylate histidine protein kinases such as EnvZ and CheA which are members of the **His-Asp phosphorelay** signal transduction systems in E. coli. Instead of ATP, the exclusive phosphodonor for histidine kinases, GTP can be utilized in vitro in the presence of NDP kinase to phosphorylate EnvZ and CheA, which then transfer the phosphoryl group to OmpR and CheY, the respective response regulators. The direct involvement of GTP for the phosphorylation of EnvZ through NDP kinase was further demonstrated by the use of a mutant EnvZ, which lost ability to be autophosphorylated with ATP. Phospho-OmpR thus formed can bind specifically to an ompF promoter sequence. These results suggest that NDP kinase may play a physiological role in signal transduction.

=>

=> s histidyl-aspartyl

L17 28 HISTIDYL-ASPARTYL

=> d his

(FILE 'HOME' ENTERED AT 12:49:11 ON 25 JUL 2000)

FILE 'MEDLINE, CAPLUS' ENTERED AT 12:49:21 ON 25 JUL 2000
L1 227 S ANTIBIOTIC# AND AUTOLYSIS
L2 0 S LYTA DEFICIENT AND L1
L3 0 S HIS-ASP AND L1
L4 132 S BACTER? AND L1
L5 28 S AUTOLYSIN DEFICIENT
L6 9 S ANTIBIOTIC# AND L5
L7 6 DUP REM L6 (3 DUPLICATES REMOVED)
L8 144 S LYTA OR LYR A
L9 139 S LYTA OR LYT A
L10 13 S ANTIBIOTIC# AND L9
L11 9 DUP REM L10 (4 DUPLICATES REMOVED)
L12 1 S (LACK? OR DEFECT?) AND L11
L13 501 S HIS-ASP
L14 36 S PHOSPHORELAY AND L13
L15 8 S (LACK? OR DEFEC? OR ABSEN?) AND L14
L16 4 DUP REM L15 (4 DUPLICATES REMOVED)
L17 28 S HISTIDYL-ASPARTYL

=> s (lack? or defec? or absen?) and l17

L18 5 (LACK? OR DEFEC? OR ABSEN?) AND L17

=> dup rem l18

PROCESSING COMPLETED FOR L18
L19 4 DUP REM L18 (1 DUPLICATE REMOVED)

=> d l19 1-4 bib ab

L19 ANSWER 1 OF 4 MEDLINE
AN 1999030824 MEDLINE
DN 99030824
TI Reconstitution of retrograde transport from the Golgi to the ER in vitro.
AU Spang A; Schekman R
CS Department of Molecular and Cell Biology and Howard Hughes Medical Institute, University of California, Berkeley, California 94720, USA.
SO JOURNAL OF CELL BIOLOGY, (1998 Nov 2) 143 (3) 589-99.
Journal code: HMV. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199902
AB Retrograde transport from the Golgi to the ER is an essential process. Resident ER proteins that escape the ER and proteins that cycle between the Golgi and the ER must be retrieved. The interdependence of anterograde and retrograde vesicle trafficking makes the dissection of both processes difficult in vivo. We have developed an in vitro system that measures the retrieval of a soluble reporter protein, the precursor of the yeast pheromone alpha-factor fused to a retrieval signal (HDEL) at its COOH terminus (Dean, N., and H.R.B Pelham. 1990. J. Cell Biol. 111:369-377). Retrieval depends on the HDEL sequence; the alpha-factor precursor, naturally **lacking** this sequence, is not retrieved. A full cycle of anterograde and retrograde transport requires a simple set of purified cytosolic proteins, including Sec18p, the Lma1p complex, Uso1p, coatomer, and Arf1p. Among the membrane-bound v-SNAP receptor (v-SNARE) proteins, Bos1p is required only for forward transport, Sec22p only for retrograde trafficking, and Bet1p is implicated in both avenues of transport. Putative retrograde carriers (COPI vesicles) generated from Golgi-enriched membranes contain v-SNAREs as well as Emp47p as cargo.

L19 ANSWER 2 OF 4 MEDLINE DUPLICATE 1
AN 97115827 MEDLINE
DN 97115827
TI Nucleoside-diphosphate kinase-mediated signal transduction via **histidyl-aspartyl** phosphorelay systems in Escherichia coli.
AU Lu Q; Park H; Egger L A; Inouye M
CS Department of Biochemistry, Robert Wood Johnson Medical School, Piscataway, New Jersey 08854, USA.
NC GM19043 (NIGMS)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Dec 20) 271 (51) 32886-93.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199703
EW 19970304
AB Nucleoside-diphosphate kinase (NDP kinase), a key enzyme in nucleotide metabolism, is also known to be involved in growth and developmental control and tumor metastasis suppression. Interestingly, we find that

coexpression of N[redacted] kinase with Taz1, a Tar/EnvZ chimera, in the **absence** of its na[redacted]ve signal, can activate a porin[redacted]ne ompC-lacZ expression in Escherichia coli. Further studies show that NDP kinase can act as a protein kinase to phosphorylate histidine protein kinases such as EnvZ and CheA which are members of the His-Asp phosphorelay signal transduction systems in E. coli. Instead of ATP, the exclusive phosphodonor for histidine kinases, GTP can be utilized in vitro in the presence of NDP kinase to phosphorylate EnvZ and CheA, which then transfer the phosphoryl group to OmpR and CheY, the respective response regulators. The direct involvement of GTP for the phosphorylation of EnvZ through NDP kinase was further demonstrated by the use of a mutant EnvZ, which lost ability to be autophosphorylated with ATP. Phospho-OmpR thus formed can bind specifically to an ompF promoter sequence. These results suggest that NDP kinase may play a physiological role in signal transduction.

L19 ANSWER 3 OF 4 MEDLINE
AN 95014711 MEDLINE
DN 95014711
TI Retrieval of HDEL proteins is required for growth of yeast cells.
AU Townsley F M; Frigerio G; Pelham H R
CS MRC Laboratory of Molecular Biology, Cambridge, United Kingdom..
SO JOURNAL OF CELL BIOLOGY, (1994 Oct) 127 (1) 21-8.
Journal code: HMV. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-X75780
EM 199501
AB The ERD2 gene of Saccharomyces cerevisiae encodes the receptor which retrieves HDEL-containing containing ER proteins from the Golgi apparatus. Viable erd2 mutants have been isolated that show no obvious HDEL-dependent retention of the luminal ER protein BiP, suggesting that retrieval of HDEL proteins is not essential for growth. However, cells that **lack** Erd2p completely have a **defective** Golgi apparatus and cannot grow. This observation led to the suggestion that the receptor had a second function, possibly related to its ability to recycle from Golgi to ER. In this paper we investigate the requirements for Erd2p to support growth. We show that mutations that block its recycling also prevent growth. In addition, we show that all mutant receptors that can support growth have a residual ability to retrieve BiP, which is detectable when they are overexpressed. Mere recycling of an inactive form of the receptor, mediated by a cytoplasmic KKXX sequence, is not sufficient for growth. Furthermore, saturation of the receptor by expression of an HDEL-tagged version of pro-alpha factor inhibits growth, even of strains that do not show obvious BiP retention. We conclude that growth requires the HDEL-dependent retrieval of one or more proteins, and that these proteins can be recognized even under conditions where BiP is secreted. Genetic screens have failed to identify any one protein whose loss could account for the Erd2p requirement. Therefore, a growth may require the retention of multiple HDEL proteins in the ER, or alternatively the removal of such proteins from the Golgi apparatus.

L19 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2000 ACS
AN 1986:474775 CAPLUS
DN 105:74775
TI Peptide synthesis catalyzed by aminoacyl-tRNA synthetase (ARS)
AU Tsurutani, Ryoichi; Nakajima, Hiroshi; Kitabatake, Senji; Tomioka, Isao;

Dombou, Munehiko; [redacted]omita, Kosuke; Imahori, Kazutom[redacted]
CS Res. Dev. Cent., [redacted]tika Ltd., Kyoto, 611, Japan
SO Pept. Chem. (1986), Volume Date 1985, 23rd, 147-52
CODEN: PECHDP; ISSN: 0388-3698
DT Journal
LA English
AB Four aminoacyl-tRNA synthetases (**histidyl-**, **aspartyl-**, leucyl-, and tyrosyl-tRNA synthetases) purified from Bacillus stearothermophilus catalyzed the formation of dipeptides in relatively good yield. The reaction was nonspecific for the amino acid used as nucleophile. The peptide formation reaction is very similar to the hydroxamate formation reaction in terms of Km values for AA1 (the amino acid specific for the synthetase) and ATP. However the Km values for AA1 are quite different between the peptide formation and aminoacyl tRNA formation reactions. The peptide formation reaction showed a **lack** of specificity for amino acid enantiomers.

=> log h

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